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EXAMINER NIGIN, RUSSELL SCOTT				
ART UNIT		PAPER NUMBER		
1631				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

Office Action Summary

Application No.

10/533,479

Applicant(s)

KARLSEN ET AL.

Examiner

Russell S. Negin

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 September 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 40-77 is/are pending in the application.
- 4a) Of the above claim(s) 41 and 55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 40, 42-54 and 56-77 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-06)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Comments

In view of the arguments filed on 3 September 2010, PROSECUTION IS HEREBY REOPENED. Additional grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Claims 41 and 55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12 February 2008.

Consequently, claims 40-77 are pending in the instant application; claims 40, 42-54, and 56-77 are examined in the instant Office action.

Withdrawn Rejections

ALL of the rejections are withdrawn in view of Remarks on pages 6-25 of the Appeal Brief filed by applicant on 3 September 2010.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection is newly applied:

35 U.S.C. 103 Rejection #1:

Claims 40, 42-43, 45-50, 56-59, 61, and 69-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blatt et al. [US Patent 4,761,381; issued 2 August 1988; on IDS] in view of Mathies et al. [US PGPUB 2002/0068357; published 6 June 2002; filing and benefit date 9 August 2001; on IDS].

Claim 40 is drawn to a microfabricated device for fragmenting nucleic acids present in a fluid sample, the device comprising an inlet port, a fragmentation cell, and an outlet port downstream from said inlet port, wherein the cell is in fluid communication with the ports, and wherein the outlet port is dimensioned to impede the flow of a fluid sample out of the cell so as to effect shearing of nucleic acid molecules therein, wherein the fragmentation cell comprises a chamber having a bottom well being generally perpendicular to the direction of flow of fluid through the outlet port, and wherein the fragmentation cell has a top wall in which the inlet port is formed, and side walls which extend from the top wall to the bottom wall, and wherein the side walls taper inwardly to meet the inlet port.

The document of Blatt et al. studies a volume metering capillary gap device for applying liquid to a reactive surface [title]. Attention is directed to Figure 9 of Blatt et al. for illustrations of many structural features of claim 40. Specifically, label 57 of Figure 9 of Blatt et al. corresponds to the inlet port for a sample. The sample then flows into the sample cell (label 58 of Figure 9 of Blatt et al.) and has its flow impeded in a microchannel (label 60 of Figure 9 of Blatt et al.) leading to an output port (label 56 of Figure 9 of Blatt et al.). Consequently, the "cell" in Figure 9 of Blatt et al. has fluid communication between all ports wherein the output port is downstream from the input

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port. The narrowing of sample cell 58 of Figure 9 of Blatt et al. to both receive the sample from inlet port 57 and output the sample via the microchannel 60 (that leads to an output port) is interpreted to meet the structural limitations of both the top and bottom walls because sample cell 58 tapers inwardly to meet the input port 57 in a way such that this "tapering" leads to a wall that is also "generally" perpendicular to the flow of the sample from sample cell 58 to the output port 56 via microchannel 60.

However, Blatt et al. does not teach that the sample cell is a nucleic acid fragmentation cell.

The document of Mathies et al. is a miniaturized and integrated nucleic acid processing and analysis device [title]. Specifically, the last 5-6 lines of paragraph 136 of Mathies et al. details how forcing nucleic acid molecules through narrow channels at relatively high velocities causes shearing and fragmentation of the nucleotides.

Claim 42 is further limiting wherein the fragmentation cell is generally pear shaped.

Figure 9 of Blatt et al. illustrates a pear shaped fragmentation cell (Label 58).

Claim 43 is further limiting wherein the width of the fragmentation cell abruptly decreases.

Claim 45 is further limiting wherein the outlet port is approximately in the middle of the bottom wall.

Claim 46 is further limiting wherein the side walls taper inwardly to meet the outlet port.

Claim 47 is further limiting wherein the bottom wall is adjacent and substantially perpendicular to the two side wall portions.

Label 58 of Figure 9 of Blatt et al. illustrates a sample chamber that abruptly decreases to meet the microchannel 60 that leads to the output port 56. The microchannel label 60 is approximately in the middle of the bottom wall wherein the sides of label 58 taper inwardly to meet the microchannel. Additionally, microchannel label 60 is substantially perpendicular to two side wall portions of chamber label 58.

Claims 48 and 49 of the instant application are further limiting wherein the side walls taper to meet the inlet port and the angle formed is less than 90 degrees.

Since Figure 9 of Blatt et al. is pear shaped and not rectangular, the angle with which chamber 58 of Blatt et al. meets inlet port 57 of Blatt et al. is slightly less than 90 degrees.

Claim 50 is further limiting wherein the geometry of the outlet port with respect to the bottom wall is described.

In Figure 9 of Blatt et al. the walls of chamber 58 taper inwardly to both meet inlet port 57 and microchannel 60 (that leads to the outlet port) such that microchannel 60 is approximately at the mid-point and the bottom wall is substantially perpendicular to the axis of the output port.

Claim 56 is further limiting comprising an access channel in fluid communication with the inlet port.

Claim 57 is further limiting comprising a collection means in communication with the outlet port.

In Figure 9 of Blatt et al., microchannel 60 communicates input liquid with collection means 61 which is in communication with an output port.

Claim 58 is further limiting wherein flow of the sample is affected by flow through the device.

Paragraph 136 of Mathies et al. teaches that the nucleotides of sample solution are fragmented when travelling through channels.

Claim 59 is further limiting wherein flow is effected using a pump.

Column 11, lines 13-26 of Blatt et al. uses vacuums and pressure to regulate flow of sample through the device.

Claim 61 is further limiting wherein the substrate and the overlying cover and a recess are present.

Figure 9 of Blatt et al. illustrates a substrate attached to an overlying cover with recesses for input and output of fluids.

Claim 69 is further limiting wherein the device fragments biological fluids.

Claim 71 is further limiting comprising the analysis biological samples.

Claim 72 is further limiting comprising an assay kit for the analysis of biological samples.

Claim 73 is further limiting wherein the device is disposable.

Since the combination of Figure 9 of Blatt et al. and Mathies et al. teach all of the structural embodiments of the instant claims, it is interpreted that since all of the structural embodiments have been taught, this structure may perform these intended uses of fragmenting biological fluids and analyzing biological sample. It is also interpreted that the device in Figure 9 of Blatt et al. may be discarded.

Claims 70 and 75 are further limiting wherein the fragmented nucleotides undergo amplification.

The abstract of Mathies et al. teaches the use of a microdevice in amplification of nucleic acids.

Claim 74 is further limiting and is a method for fragmenting nucleic acids using the provided apparatus involving pumping a sample through the device and collecting the resultant fluids.

As explained above, Figure 9 of Blatt et al. teaches all of the structural aspects of the recited microdevice except a cell for fragmentation. The document of Mathies et al.

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teaches this fragmentation both structurally (within channels) and as a method (paragraph 136).

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the microreactor of Figure 9 of Blatt et al. such that it contains a fragmentation (narrowed) channel for the purpose of shearing nucleic acids as described in paragraph 136 of Mathies et al. because it is obvious to combine known elements in the prior art to yield a predictable result. In this instance, the device and method of Mathies et al. is an alternative structure utilizing a constricting microdevice (i.e. for the application of fragmenting nucleic acids). There would have been a reasonable expectation of success in combining Blatt et al. with Mathies et al. because both devices analogously pertain to microreactors with similar constricting structures and functions.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #2:

Claims 44, 51-53, 64-66, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blatt et al. in view of Mathies et al. as applied to claims 40, 42-43, 45-50, 56-59, 61, and 69-75 above, in further view of Gilmanshin et al. [US PGPUB 2001/0014850; published 16 August 2001].

Claim 44 is further limiting wherein the dimensions of this constriction are recited.

Claims 51-53 are further limiting wherein there is an obstacle in the cell that bifurcates flow of the liquid.

Claims 64 and 66 are further limiting comprising a plurality of serially connected chambers.

Claim 65 is further limiting wherein there is a third fragmentation cell.

Claim 77 is further limiting wherein the constriction width is from 5 to 50 microns.

The documents of Blatt et al. and Mathies et al. make obvious a microdevice for fragmenting nucleic acids comprising narrow channels for shearing, as discussed above. Blatt et al. and Mathies et al. also teach in Figure 9 of Blatt et al. that the flow is substantially perpendicular to the axis of the outlet.

Blatt et al. and Mathies et al. do not teach or suggested the recited constriction dimensions. Blatt et al. and Mathies et al. also do not teach serial connections of pluralities of reaction chambers.

The document of Gilmanshin et al. studies uses of microchannels to analyze polymeric solutions [Figure 8 of Gilmanshin et al.]. Specifically, paragraph 119 teaches using such elongation regions of Figure 8 of Gilmanshin et al. in series such that a plurality (two or more) channel structures are connected in series. Paragraph 119 and Figure 8 of Gilmanshin et al. also teach that a subset of the channels contain obstructions (obstacles) that bifurcates the fluid path of the sample. Additionally, Figure 9 of Gilmanshin et al. teaches the dimensions of the constriction recited in the instantly rejected claims.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the microreactors of Blatt et al. and Mathies et al. by use of the diverse elongation reactors with the dimensions listed in Gilmanshin et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the microchannels in Gilmanshin et al. are alternate microdevices as those listed in Blatt et al. and Mathies et al. In addition, connecting multiple reactors in series (as in Gilmanshin et al.) is an alternative to flowing solution through a single reactor (as in Blatt et al. and Mathies et al.). There would have been a reasonable expectation of success in combining Blatt et al., Mathies et al., and Gilmanshin et al. because all three studies analogously pertain to structure of microchannels with the function flowing a solution through them.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #3:

Claims 60, 62-63, and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blatt et al. in view of Mathies et al. as applied to claims 40, 42-43, 45-50, 56-59, 61, and 69-75 above, in further view of Wilding et al. [US Patent 5,304,487; issued 19 April 1994].

Claim 60 is further limiting wherein the chamber comprises a variable volume.

Claim 62 further limits the type of materials of the cover and substrate. Claim 63 and 76 are further limiting wherein the glass cover is bound to the substrate.

The documents of Blatt et al. and Mathies et al. make obvious a microdevice for fragmenting nucleic acids through shearing, as discussed above.

Blatt et al. and Mathies et al. do not teach variable volumes wherein the substrate is silicon and there is a glass cover anodically bound to the substrate.

The document of Wilding et al. studies fluid handling in analytical devices [title]. Specifically, column 6, line 8-21 of Wilding et al. teach a silicon substrate that is anodically bound to a glass cover to result in flow channels with varying widths and depths.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the microreactors of Blatt et al. and Mathies et al. by use of the silicon substrate with anodically bound glass as in Wilding et al. wherein the motivation would have been that the configuration of Wilding et al. yields transparency (in terms of observing the sample through glass) and flexibility (in terms of regulating the dimensions of the device) [column 6, lines 8-21 of Wilding et al.].

The following rejection is newly applied:

35 U.S.C. 103 Rejection #4:

Claims 54 and 67-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blatt et al. in view of Mathies et al. in view of Gilmanshin et al. as applied to claims 40, 42-53, 56-59, 61, 64-66, 69-75, and 77 above, in further view of Wilding et al.

Claim 54 is further limiting in which the obstacle is generally triangular.

Claims 67-68 are further limiting wherein the size of the outlet port decreases sequentially along the fragmentation cell.

The documents of Blatt et al., Mathies et al., and Gilmanshin et al. make obvious a microdevice for fragmenting nucleic acids through shearing wherein there are microchannels connected in series, as discussed above. While Gilmanshin et al. teaches obstructions to flow, Blatt et al., Mathies et al., and Gilmanshin et al. do not teach triangular obstructions with the configurations recited in claim 54. Blatt et al., Mathies et al., and Gilmanshin et al. also do not teach sequential decreases in size of outlet ports.

The document of Wilding et al. studies fluid handling in analytical devices [title]. Specifically, Figure 1 of Wilding et al. teaches triangular obstructions (label 24). Furthermore, the microdevice of Wilding et al. comprises a system of microchannels connected in series wherein the widths gradually decrease into the center of the system.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the microreactors of Blatt et al. and Mathies et al. and the device configurations of Gilmanshin et al. by use of the triangular obstacles and systems of channels with decreasing widths as in Wilding et al. because it is obvious to combine known elements in the prior art to yield a predictable result. In this instance, the types of obstructions and channel systems of Wilding et al. are alternate forms of the configurations used in Blatt et al., Mathies et al., and Gilmanshin et al. There would have been a reasonable expectation of success in combining Blatt et al., Mathies et al.,

Gilmanshin et al., and Wilding et al. because all of the studies pertain to analyzing a sample as it flows sequentially through analogous structural microdevices that impose shear as a result of constricting microchannels.

Response to Arguments

Applicant's arguments with respect to the instantly rejected claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 8:30 am to 5:30 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/
Russell S. Negin
15 November 2010

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631